(b) inhaling the aerosol into the respiratory tract of the subject, wherein [the] an aerodynamic diameter of the particles target the particles to the specified region of the respiratory tract.

a 1

2. (Amended) The method of claim 1, wherein the aerodynamic diameter range of the particles is [in the range of] about 1-3 μm, and the [specified region of the respiratory tract] end location is the alveoli.

3. (Amended) The method of claim 1, wherein the aerodynamic diameter range of the particles is [in the range of] about 4-6 μm, and the [specified region of the respiratory tract] end location is the central airways.

4. (Amended) The method of claim 1, wherein the aerodynamic diameter range of the particles is [in the range of] about 7-10 μm, and the [specified region of the respiratory tract] end location is the upper respiratory tract.

a 2

8. (Amended) The method of claim 1, wherein the formulation is an aqueous solution and the method further comprises heating, prior to said aerosolizing, in an amount [significant] sufficient to evaporate water away from the solution thereby adjusting particles.

a 3

17. (Amended) A method of delivering a polynucleotide preferentially to a specified region of a respiratory tract in a mammalian subject comprising:

(a) determining an inspiratory volume of the subject;

(b) calibrating a delivery device based on the inspiratory volume determined in step (a);

[(b)] (c) aerosolizing a formulation comprising a polynucleotide, thereby forming aerosolized particles [having an aerodynamic diameter related to the diameter of airways in an area of a respiratory tract of the subject];

[(c)] (d) inhaling the aerosolized particles into the respiratory tract of the subject, wherein [the] an aerodynamic size of the particles target the particles to the specified region of the respiratory tract [is related to the diameter of airways in the specified region of the respiratory tract]; and

[(d)] (e) repeatedly aerosolizing the ~~polynucleotide formulation at the same~~ determined inspiratory volume.

20. (Amended) A method of delivering a polynucleotide preferentially to a specified region of a respiratory tract in a mammalian subject, comprising:

(a) determining an aerodynamic diameter range of particles comprising a polynucleotide to be delivered, based on whether a desired end location of travel is the upper respiratory tract, the central airways, or the alveoli;

(b) aerosolizing a liquid formulation comprising [a polynucleotide] the particles and a lipid carrier [, thereby forming aerosolized particles having an aerodynamic diameter related to the diameter of airways in an area of a respiratory tract of the subject]; and

(b) inhaling the aerosol into the respiratory tract of the subject, wherein the aerodynamic diameter of the particles targets the particles to the specified region of the respiratory tract.

II. REMARKS

Formal matters

Claims 1-20 are pending in this application after entry of the amendments set forth above.

Claims 1-20 were examined and were rejected.

Claims 1-4, 8, 17 and 20 are amended for clarity, and to more particularly point out and distinctly claim the invention. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1-4, 8, 17 and 20 is found in the claims as originally filed, and throughout the specification, in particular at the following locations: page 5, line 21 - page 6, line 5; page 23, line 9 - page 24, line 4; and page 28, lines 11-26. Accordingly, no new matter is added by these amendments.